MARKED-UP COPY OF AMENDED CLAIMS:

1. (AMENDED) A pharmaceutical composition for oral administration to a mammalian subject, comprising:

a) a taxane or taxane derivative as active ingredient;

b) a vehicle comprising at least 30% by weight of a carrier for the taxane, said carrier having an HLB value at least about 10~~.~~; wherein the vehicle additionally comprises about 5-70% by weight of a co-solubilizer which reduces the viscosity of the vehicle.

4. (AMENDED) A composition according to claim 3 wherein said saturated ~~polyglycolized~~ polyglycolyzed glycerides include glycerides of C_8 - C_{18} fatty acids.

13. (AMENDED) A composition according to claim ~~12~~1 wherein the co-solubilizer is capable of solubilizing at least about 25 mg/ml of the taxane at about 20-25°C.

14. (AMENDED) A composition according to claim ~~12~~1 wherein the vehicle comprises about 10 - 50% by weight of the co-solubilizer.

15. (AMENDED) A composition according to claim ~~12~~1 wherein the co-solubilizer is selected from the group consisting of N-methyl-2-pyrrolidone, glycerol or propylene glycol esters of caprylic and capric acids, polyoxyethylated hydroxystearates, polyoxyethylated sorbitan esters, polyethylene glycol esters of caprylic and capric acids, modified castor oils, vegetable oils, ~~such as olive oil,~~ saturated polyglycolyzed glycerides, citrate esters, propylene glycol, ethanol, water and lower molecular weight polyethylene glycols.

21. (AMENDED) A composition according to claim 3 wherein the ~~carrier~~ surfactant or emulsifier~~comprises~~ is Vitamin E TPGS.

22. (AMENDED) A composition according to claim 4 wherein the ~~carrier comprises~~ saturated polyglycolyzed glycerides ~~of~~ are C_8 - C_{18} fatty acids.

24. (AMENDED) A composition according to claim 3 wherein the ~~carrier comprises~~ surfactant or emulsifier is selected from polyoxyethylated stearate esters.

REMARKS

Claims 1 to 117 were pending. Claim 12 is cancelled without prejudice. Claims 1, 4, 13 to 15, 21, 22, and 24 are amended and new claim 118 is added. Upon entry of this Amendment, claims 1 to 11 and 13 to 118 will be under examination.

The recitations of Claim 12 have been incorporated into Claim 1. Claim 12 has been cancelled and the dependencies of Claims 13-15 have been changed accordingly. The amendments to claims 4, 21, 22 and 24 involve correcting typographical errors or informalities. Support for new claim 118 can be found in the original claim 15. Therefore, the amendments to claims 1, 4, 13 to 15, 21, 22, and 24, and the addition of new claim 118 are fully supported by the original specification and do not raise any issue of new matter. Accordingly, entry of this Amendment is respectfully requested.

RESTRICTION REQUIREMENT

Claims 53 to 117 stand withdrawn from further consideration as being drawn to a non-elected invention on the ground that the compositions defined by Claims 1-52 have uses other than those defined by Claims 53-117. No such uses have been put forth on the record, however. Plainly, treating taxane-responsive diseases would appear to be the primary use of the compositions. In addition, the search required for the compositions would seem co-extensive with the search for the method. Reconsideration and withdrawal of this requirement are respectfully requested.

REJECTION OF CLAIMS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1, 2, 8 to 20 and 25 to 52 stand rejected under 35 U.S.C. §112, first paragraph, as non-enabled for any and all carriers defined in terms of having an HLB value of at least about 10, on the ground that the absorption of a taxane is "unpredictable and unexpected". The Office Action does acknowledge that the specification is enabling for specific surfactants and emulsifiers without naming them. Applicants

submit that the claimed invention is fully enabled by the present specification as it pertains to recited carriers.

As the Examiner has correctly pointed out, the recited carriers promote absorption of the taxane in addition to acting as suitable solvents. See, pages 9-10 of the specification. This disclosure also indicates that not all carriers exhibit these properties, only carriers having an HLB value of at least about 10. Plainly, the determination of the HLB value of a given carrier does not involve undue experimentation. Numerous working examples of carriers, including Vitamin E TPGS and members of the GELUCIRE, LABRASOL, CREMOPHOR EL OR RH40, TWEEN, CRILLET, BRIJ, CROVOL, EMSORB and SOLUTOL families of carriers, and beta-cyclodextrins, are provided. See, page 10, lines 5 to 17 of the specification. In addition, 21 working examples of carrier substances are set forth on table 2 (page 23) of the specification. Example 1 on pages 21-22 describes an animal screening model for selecting carriers that provide the requisite properties. Tables 3 to 11 on pages 24-30 provide many more working examples of the claimed pharmaceutical compositions. Data contained in these tables were generated using the animal-screening model. In sum, the present specification provides a criterion for selecting carriers, numerous working examples and a test for identifying yet other carriers suitable for use in the claimed invention. Thus, Applicants submit that the claims are fully enabled by the present specification. The Examiner is respectfully reminded that applicant need not describe all actual embodiments (MPEP 2164.02) nor must the claims be limited to preferred embodiments in the specification (*In re Goffe*, 191 U.S.P.Q. 429, 431 (CCPA 1976)). Reconsideration and withdrawal of the rejection are respectfully requested.

REJECTION UNDER 35 U.S.C. §103(a)

Claims 1 to 52 have been rejected under 35 U.S.C. §103(a) as being unpatentable over any of Bastard *et al.*, U.S. Patent 5,403,858 ("*Bastard*"), Agharkar *et al.*, U.S. Patent 5,504,102 ("*Agharkar*"), Bobee *et al.*, U.S. Patent 5,438,072

("*Bobee*"), Schwartz *et al.*, U.S. Patent 5,610,173 ("*Schwartz*"), Kaufman *et al.*, U.S. Patent 5,616,330 ("*Kaufman*"), Benet *et al.*, U.S. Patent 5,665,386 ("*Benet*"), Trissel *et al.*, U.S. Patent 5,681,846 ("*Trissel*"), and Anderson *et al.*, U.S. Patent 5,877,205 ("*Anderson*"). The Office Action states that in the absence of a clear delineation of the present compositions, particularly with respect to the broadly defined carriers, and a showing of unexpected properties resulting from any such differences, no patentable significance is seen in the present invention.

Reconsideration and withdrawal of this rejection are respectfully requested because none of the cited references teaches or suggests the claimed pharmaceutical composition. The claimed invention achieves unexpectedly high bioavailability when orally administered to a mammal.

Bastard discloses a taxane composition comprising a taxane and a polyethylene glycol or a hydrogenated castor oil. *Agharkar* teaches the preparation of a composition containing a taxane and a mixture of ethanol and a polyoxyethylated castor oil. *Bobee, Schwartz, Kaufman* and *Trissel* describe the use of surfactants in a taxane composition. *Anderson* discloses the use of polyethylene glycol in a taxane composition. *Benet* teaches the use of essential oil in compositions containing oral pharmaceutical compounds. However, this *Benet* publication does not teach or suggest taxanes.

There is no disclosures in any of these cited references of the specific combination of a taxane, a carrier having an HLB value at least about 10 and 5-70% of a co-solubilizer.

In addition, the claimed taxane composition achieves unexpectedly high rates of bioavailability upon oral administration. For example, in a taxane composition comprising POE 40 stearate ester as the carrier and Pharmasolve as the co-solubilizer as described in line 2 of table 5 of the specification, a taxane bioavailability of 57.3% compared with that of intravenous injection was achieved upon oral

administration of the composition. Numerous other examples also show that taxane is absorbed at an unexpectedly high rate upon oral administration of the claimed taxane composition, taxane dosage form, or the two-part taxane medicament. With the exception of *Benet*, the cited prior art deals exclusively with intravenous administration. There is no suggestion in the prior art teachings that compositions embraced by the present claims would achieve such results.

Therefore, claims 1 to 11 and 13 to 52, as amended, would have been nonobvious over any or the combination of *Bastard, Agharkar, Bobee, Schwartz, Kaufman, Benet, Trissel*, and *Anderson*. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

In view of the amendments and the remarks, further and favorable action in the form of a Notice of Allowance with respect to claims 1 to 11 and 13 to 118 is respectfully requested.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Respectfully submitted,

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